May-Thurner Syndrome

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ABSTRACT

This single-center, retrospective review identified 6 patients ($n = 6$, 100% female) treated by endovascular therapy for May-Thurner syndrome from June 2013 to September 2015. Patients consisted of 3 African American, 2 Caucasian and 1 Asian; mean age was 53.50 ± 8.31 years, range: 39-63 years. Clinical presentations consisted of left lower extremity deep vein thrombosis in 4, left lower extremity deep vein thrombosis with pulmonary embolism in 1 and pulmonary embolism with left common iliac vein thrombosis in 1 patient. All 6 patients were treated with catheter-directed thrombolysis and venous stenting to correct the underlying anatomical defect. Hypercoagulability work up revealed antiphospholipid antibody syndrome in 1 patient. No major periprocedural complications were observed. Median follow-up period was 22 ± 5.5 months (range: 13-30 months). One patient with pre-exiting antiphospholipid antibody syndrome developed stent thrombosis with secondary loss of patency. Endovascular therapy for May-Thurner syndrome in our adult cohort seemed safe and effective. One patient with pre-existing thrombophilia developed secondary loss of stent patency, suggesting need for further investigation in this subgroup.

Key Indexing Terms: May-Thurner syndrome; Deep vein thrombosis; Pulmonary embolism and endovascular treatment; Pharmaco-mechanical thrombolysis. [Am J Med Sci 2018;355(5):510–514.]

INTRODUCTION

May-Thurner syndrome (MTS) is an anatomical defect described as an external compression of left common iliac vein (CIV) by right common iliac artery (CIA) against the pelvic brim and the fifth lumbar vertebra[1] leading to symptoms of impaired venous outflow from the left lower extremity (LLE). Long-standing compression by a pulsatile artery causes intimal fibrosis leading to venous spur formation. This results in mechanical obstruction to venous flow, which causes increased risk of LLE deep vein thrombosis (DVT), chronic venous stasis and venous hypertension. It is not uncommon to find left CIV compression by right CIA on imaging in asymptomatic patients.[2] Radiologic studies have reported up to 24% prevalence of greater than 50% compression of left CIV by right CIA.[2] This anatomical abnormality has a reported prevalence of 20-34% in cadaveric studies.[1] The occurrence of the LLE DVT[3] is 5 times more common and is believed to be related to this anatomic defect; however, only 2-3% of LLE DVTs are reported as related to MTS.[1,2] Such under diagnosis is probably because workup is generally stopped once the diagnosis of DVT is confirmed. In this case series, we describe 6 cases of MTS presenting with LLE DVT and pulmonary embolism (PE). All 6 cases were treated with thrombolysis, anticoagulation and correction of anatomical defect by angioplasty.

CASE PRESENTATIONS

Cases

Formal, informed consent was obtained from each individual patient per institutional policy and approval from the institutional review board was obtained. A retrospective review of the picture archiving and communication system radiology database was done using May-Thurner syndrome as the keyword. We identified 6 patients above the age of 18 who underwent endovascular therapy for MTS from June 2013 to September 2015. Patients who had endovascular intervention or stent placement in the lower extremity venous system before initial presentation to our institution were excluded because of lack of information pertaining to initial presentation, procedural details and postprocedural follow up.

Data including demographics, initial clinical presentation, modality of diagnosis and details of endovascular intervention were obtained. Postprocedural follow-up

TABLE 1. Demographic characteristics of study cohort.

Case number	Age	Sex	Race	Weight, kg	Height, cm	BMI, kg/m^2	Obstetric index
1	53	F	AA	100	167	35	P3L3
2	52	F	AA	90	160	34	P4L4
3	39	F	Asian	72	157	31	P2L2
4	54	F	Caucasian	57	155	23	P5l5
5	60	F	Caucasian	70	160	27	P3L3
6	63	F	AA	112	175	36	P5L5

AA, African American; BMI, body mass index.

data were obtained from primary care physicians' records and symptoms were quantified by Villalta score (VS).[17] Data were entered on Microsoft Excel Spreadsheet and was converted to SPSS PC+ 16 version for statistical analysis. Continuous variables are expressed as mean, standard deviation and categorical data were presented as absolute values and percentages.

Our study cohort consisted of 6 female and 0 male patients with 3 of African American, 2 Caucasian and 1 of Asian origin. Mean age was 53.50 ± 8.31 years (ranged from 39-63 years). Mean weight was 83.5 kg, (range: 57-112 kg). Body mass index was 31.32 ± 5.34 kg/m^2 (range: 23.70-36.60 kg/m^2). All 6 patients were multiparous, mean parity was 3.7 ± 1.2. Demographic characteristics of the patients are summarized in Table 1.

All 6 patients were diagnosed of MTS in an inpatient setting. Case 1 presented to emergency after noting marked pain and swelling of her LLE nearly a month after right knee arthroscopic surgery. Case 3 was found to have an underlying antiphospholipid antibody (APLA) syndrome and had a history of hormonal contraceptive use. DVT was found in LLE in venous Doppler in 5 of the 6 patients. Case 4 presented with multilobar PE in the absence of thrombus in bilateral lower extremity veins. Computed tomographic (CT) angiography of the chest and abdomen showed the right common iliac artery compressing the left common iliac vein associated with a thrombus within the left common iliac vein. Cases 2 and 3 had proximal extension of the thrombus into infra renal and infra hepatic inferior vena cava (IVC), respectively. Clinical presentation, triggering risk factors and the extent of thrombosis are summarized in Table 2.

All patients except case 4 presented with clinical features including but not limited to pain and swelling of the LLE. Doppler ultrasonography revealed thrombus within the LLE venous system. It also revealed absence of respiratory variation, loss of collapsibility in femoral veins or extensive clot burden raising the suspicion for proximal obstruction. On noting 1 or more of these indirect signs at Doppler sonography, contrast-enhanced CT of the abdomen and pelvis was performed. It revealed MTS anatomy along with thrombosis (Figure 1), anatomical extent of the thrombus is summarized in Table 2.

Treatment

Following the diagnosis of DVT/PE, all 6 patients were initially treated with a protocol-driven heparin infusion. In all cases, catheter-directed thrombolysis with tissue plasminogen activator (tPA) was performed. In cases 1, 3 and 4 pharmaco-mechanical thrombolysis was additionally performed due to extensive clot burden. In cases 1 and 3 the AngioJet (Boston Scientific, Marlborough, MA) and in case 4 the Trellis (Medtronic, Minneapolis, MN) pharmaco-mechanical thrombectomy systems were utilized. In cases 2, 3, 4 and 5 retrievable IVC filter was deployed before catheter-directed thrombolysis to prevent PE. After completion of thrombolysis, balloon angioplasty of venous stenosis was performed followed by deployment of self-expanding metallic alloy stent (Wall stent, Boston Scientific, Marlborough, MA) to correct the anatomical defect (Figures 2 and 3). All 6 patients had an uneventful recovery and were

TABLE 2. Summary of clinical presentation, triggering risk factor and extent of thromboembolism.

Case number	Identified triggering risk factor	Admission diagnosis	Extent of thrombus distribution
1	None identified	LLE DVT	Left CIV to left CFV
2	Prolonged immobilization (ACL repair 3 weeks back)	LLE DVT	Infra renal IVC to left CFV
3	APLA, OCP Use	LLE DVT	Infra hepatic IVC to left CIV
4	None Identified	PE	Multilobar PE and left CIV DVT
5	None identified	LLE DVT with PE	Left CFV and left SFV and RML PE
6	None Identified	LLE DVT	Left ILV to left CFV

OCP, oral contraceptive pills; APLA, antiphospholipid syndrome; CFV, common femoral vein ; CIV, common iliac vein; DVT, deep vein thrombosis; IIV, internal iliac vein; IVC, inferior vena cava; LLE, left lower extremity; PE, pulmonary embolism; RML, right middle lobe; LLE, left lower extremity; RML, right middle lobe; SFV, superficial femoral vein.

FIGURE 1. Coronal maximum intensity projection image of the same patient shows thrombus (arrow) in the left common iliac vein propagating into the inferior vena cava.

discharged home on oral warfarin for 6 months except case 3. Case 3 had underlying APLA syndrome and was advised to use lifelong anticoagulants. Details of endovascular intervention and anticoagulation is summarized in Table 3.

Follow up

After the procedure, all 6 patients followed up with their primary care physician for a median duration of 22.00 ± 5.55 months (range: 13.00-30.00 months). Postprocedural outcomes were evaluated based on the clinical documentation of patients' primary care visit. Post-thrombotic syndrome was assessed by using VS.[17] VS was calculated from one indexed primary care visit within 6-12 months after the procedure. VS was derived from the clinical records. Any adverse clinical event was recorded from primary care provider's database. Case 2

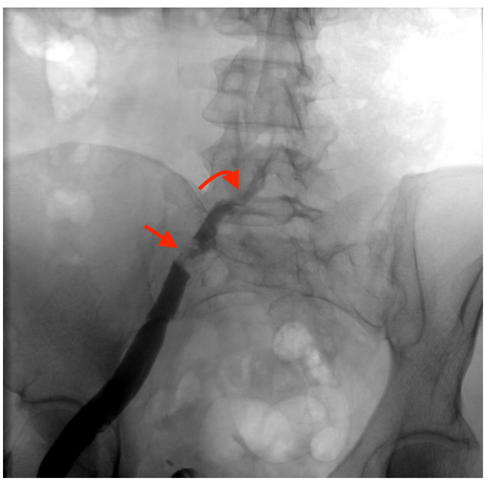

FIGURE 2. Venogram of the left lower extremity after catheter-directed thrombolysis shows residual thrombus in the left common femoral vein (arrow) as well as stenosis at the level of compression by right common iliac artery (curved arrow).

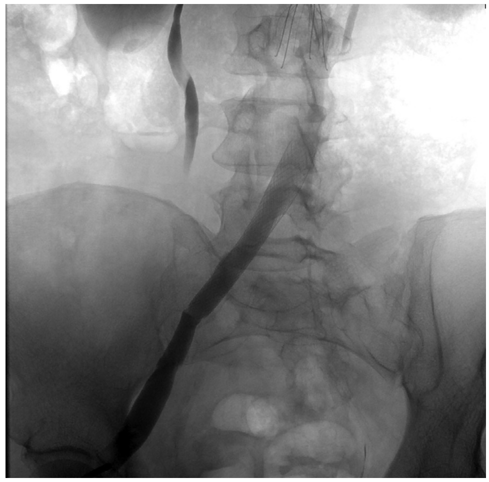

FIGURE 3. Venogram of the left lower extremity after stent placement shows good result with absence of stenosis.

was symptomatic with a VS of 2 and Case 3 had VS of 3, rests of the 4 patients were asymptomatic and had VS of 0. Postprocedural outcome is summarized in Table 4. Case 3 was admitted to a different facility with thrombosis within the previously treated iliofemoral segment 7 months after initial therapy in spite of close compliance with warfarin regimen and routinely monitored therapeutic international normalized ratio. Venous flow was reestablished by overnight infusion of tPA and she was discharged on Rivaroxaban. Rivaroxaban has been shown to have noninferior efficacy in recurrent thrombosis when compared to enoxaparin and vitamin K antagonists. However, there were no head to head trials comparing rivaroxaban to warfarin in the setting of APLA syndrome. Follow-up data is summarized in Table 4.

DISCUSSION

Rudolf Virchow described the famous Virchow's triad of thrombosis in the setting of iliofemoral DVT and venous stasis in 1851. He noted DVTs occurring 5 times more commonly in the LLE compared to the right.[3] May and Thurner[1] explained the anatomical basis for this left-sided propensity as MTS. MTS is described as the compression of the left CIV by the right CIA against the spine and pelvic brim.[1] The syndrome is reportedly seen in approximately 18-49% of patients with left-sided lower extremity DVT, more commonly involving middle-aged females.[3,4]

MTS can be a congenital or acquired anatomical variant. One common characteristic seen in our study cohort was multiple pregnancies. Physiological changes during pregnancy and labor may produce some anatomical changes of the pelvic organs. Association of MTS with multiple pregnancies and body habitus has not been previously studied. Our observation is based on a small sample size (n = 6) and multiparty may just be a baseline characteristic of the population studied.

TABLE 3. Summary of intervention and procedural data.

Case number	Access site	CDPT, agent dose and duration	IVC filter	Predeployment venoplasty	Stent
1	Left popliteal	tPA 1 mg/h for 1 day	No	Yes	16 mm × 60 mm wall stent
2	Left popliteal	tPA 0.5 mg/h for 1 day	Yes	Yes	18 mm × 90 mm wall stent
3[a]	Left popliteal	tPA 1 mg/h for 2 days	Yes	Yes	18 mm × 90 mm wall stent
4	Left popliteal	tPA 0.5 mg/h for 2 days	Yes	Yes	16 mm × 90 mm wall stent
5	Left popliteal	tPA 0.5 mg/h for 1 day	Yes	Yes	16 mm × 90 mm in IIV and 4 mm × 70 mm wall stent EIV
6	Left popliteal	tPA 0.5 mg/h for 1 day	No	Yes	16 mm × 90 mm wall stent

Note: There were no reported major periprocedural complications in any of the 6 cases. CDPT, catheter-directed pharmacologic thrombolysis; EIV, external iliac vein; IIV, internal iliac vein; IVC, inferior vena cava

[a] Second intervention after in-stent thrombosis.

Chronic compression of a vein by a large pulsatile artery against a stiff bone may produce endothelial injury leading to intimal hyperplasia. This in long-term may result in fibrotic changes within the venous wall in form of bands and spurs creating a fixed intrinsic mechanical obstruction.[5]

Mechanical obstruction limits venous drainage from LLE, producing chronic venous stasis with predisposition to thrombosis per Virchow's triad. Acute iliofemoral DVT is the most common form of presentation of MTS.[6] The risks of acute DVT are even higher in the presence of other risk factors, such as prolonged immobilization, obesity, use of hormonal contraceptives and pregnancy.[6] Patients may alternatively present with symptoms or signs related to chronic venous stasis like swelling, hyperpigmentation, stasis dermatitis and chronic venous ulcers.[6,7] Patients may present with PE in absence of LLE DVT, accounting to the pelvic venous source of embolus. Out of 6, 2 patients presented with PE. Extensive clot burden may result in excessive swelling, increasing the risk of compartmental syndrome and rarely common iliac vein perforation.[9]

The most commonly used noninvasive and cost-effective modality for the diagnosis of DVT is Doppler ultrasonography.[5] Its use is limited in evaluating iliac veins given their deep pelvic location.[5,6] Sonographic findings of the common femoral vein (CFV) can often suggest proximal obstruction. Loss of collapsibility of CFV, lack of respiratory variations and absence of response to Valsalva maneuver even in the absence of CFV thrombosis can be suggestive of a potential proximal compression or obstruction.[5]

retroperitoneal pelvic venous structures can be demonstrated at cross-sectional venography with CT and magnetic resonance venography with an excellent sensitivity and specificity.[5] All 6 cases of MTS described here were diagnosed based on CTV findings.

Digital substraction venography is the gold standard for diagnosis of MTS.[5] Typical findings include reversal of flow within the left internal iliac vein and collateral formation.[5,10] It is usually performed in combination with endovascular treatment.[5] A conservative approach such as compression stockings, tight compression bandage may be tried for symptomatic relief.[11] Several surgical techniques to correct the anatomical defect have been previously described. It includes procedures like reimplantation of the left CIV onto the vena cava, saphenous vein bypass, excision of intraluminal adhesions, and placement of the right CIA into a peritoneal sling.[12] These procedures had limited success, producing 40-88% [13] left CIV patency. Given the invasive nature of surgery, the current of standard of care is minimally invasive endovascular therapy. Surgical decompression is preferentially a second line of treatment in cases of endovascular treatment failure and technically complicated cases for endovascular approach.

Endovascular therapy for acute iliofemoral DVT includes urgent catheter-directed thrombolysis using a pharmacologic agent or a mechanical device or both. This is followed by venoplasty and common iliac venous stenting.[8] Retrievable IVC filter may be used to prevent embolization and thrombus propagation.[8,14]

Early thrombolysis may preserve valve function and prevent post-thrombotic syndrome.[8,1] Direct infusion of tPA for 12-48 hours into the thrombosed vein is used for pharmacologic thrombolysis.[8,12]

Venoplasty and venous stent are done after completion of thrombolysis.[8] Self-expanding nitinol or a stainless-

TABLE 4. Postprocedure follow-up data.

Case number	Duration, months	Stent thrombosis requiring reintervention	Villata score[17] [a]
1	30	N	0
2	24	N	2
3	23	Y[b]	3
4	22	N	0
5	20	N	0
6	13	N	0

[a] Villata score[17] is calculated from clinical documentation of patients' primary care visit within 1 year after the procedure.

[b] Case 3 developed thrombosis at of the stented vein 7 months after the initial procedure.

steel stent are used to recanalize the stenosed venous segment and sometimes IVC if required.[8,12,13,14,15] Patients are typically treated with oral anticoagulation for at least 6 months after endovascular therapy.[3,6] Primary and secondary patency rates after venous stenting are reported as high as 78% and 95% at 2-year follow-up evaluation.[13,14]

Venoplasty and venous stenting can also be used in treating MTS in the absence of thrombosis. After the procedure, these patients are generally treated with anti-platelet agents instead anticoagulants. There is no sufficient evidence in support of this approach and it is largely based on the data from arterial interventions.[16]

CONCLUSIONS

Left CIV compression by right CIA is a relatively under-diagnosed clinical entity. It should be considered as a possible cause of unexplained left-leg DVT and unexplained swelling and pain of the left leg, given its reported prevalence in cadaveric and radiological studies. Failure to recognize underlying MTS may increase the risk of recurrent venous thromboembolism, attributing to increased risk of morbidity and mortality. It is noted that all patients in our female cohort were multiparous. Given the small sample size, statistically significant causal association could not be established and it may just be a baseline characteristic of the population studied. An underlying thrombophilia in a single patient was associated with secondary loss of stent patency. Several limitations of this study need to be recognized. The total sample size was small ($n = 6$). Follow-up protocols and intervals were not standardized and the overall follow-up intervals were relatively short. Stent patency after the procedure was estimated based on clinical scoring (VS) and not by imaging. This potentiates the overestimation of patency rate in the presence of subclinical loss of patency. In conclusion, endovascular therapy for the treatment of MTS in our adult cohort was safe and effective in relieving venous obstruction. As previously reported in the literature, venous stent placement in patients with underlying thrombophilia may be associated with poorer patency rate, suggesting the need of further consideration in this subgroup.

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